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Title:	Soft matter and nanomaterials characterization by cryogenic transmission electron microscopy.
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Soft matter and nanomaterials characterization by cryogenic transmission electron microscopy.

PRESENTED BY

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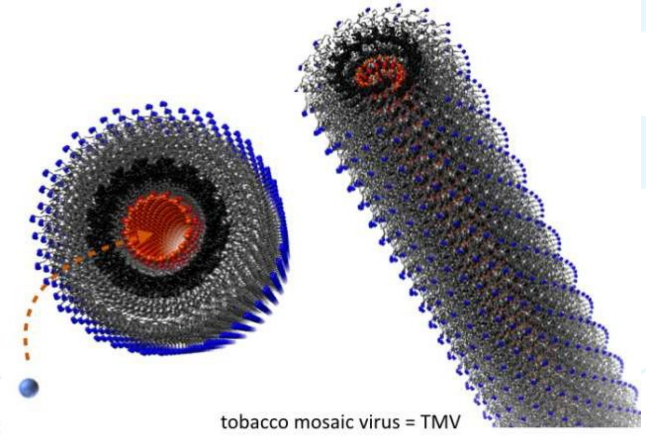
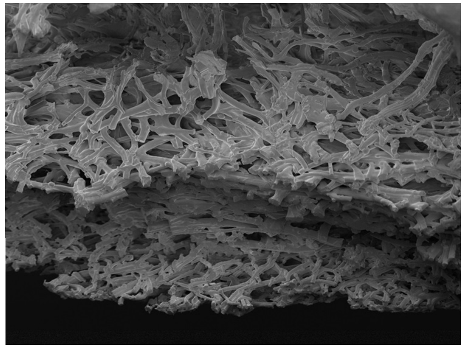
Center for Integrated Nanotechnologies
Los Alamos National Laboratory

Soft Matter and Nanomaterials

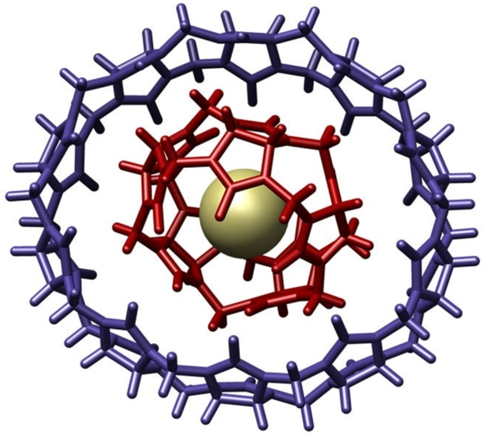
- Biological based ‘soft’ nanoparticles e.g., viruses and polymer conjugates.



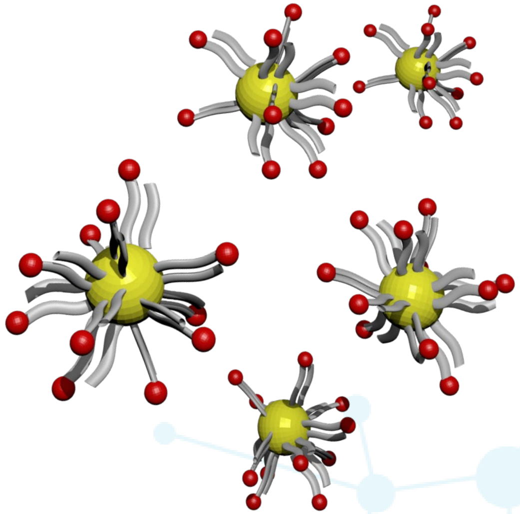
- Synthetic organic nanostructures e.g., polymers



- Supramolecular materials.



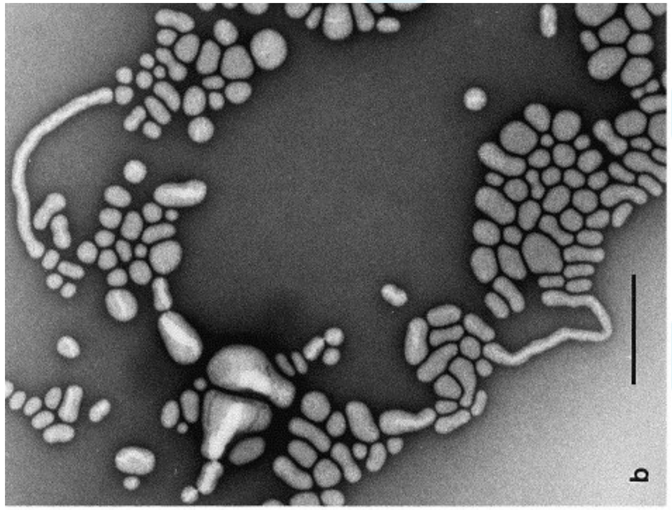
- Inorganic nanomaterials, and the inorganic-organic interface.



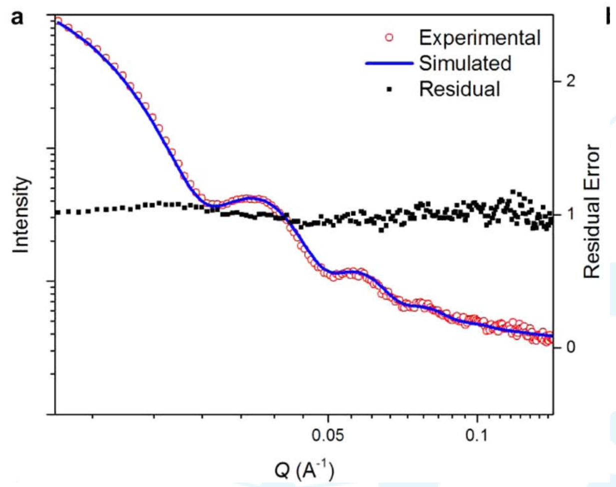
Historical Characterization of Soft Matter

- Soft matter has historically seen limited analysis by transmission electron microscopy (TEM).
  - e^- beam damage.
  - Instability under a high vacuum environment.
  - Drying artifacts.
  - Low contrast against the carbon film background.
    - Negative Staining Technique e.g., with uranyl accetate.

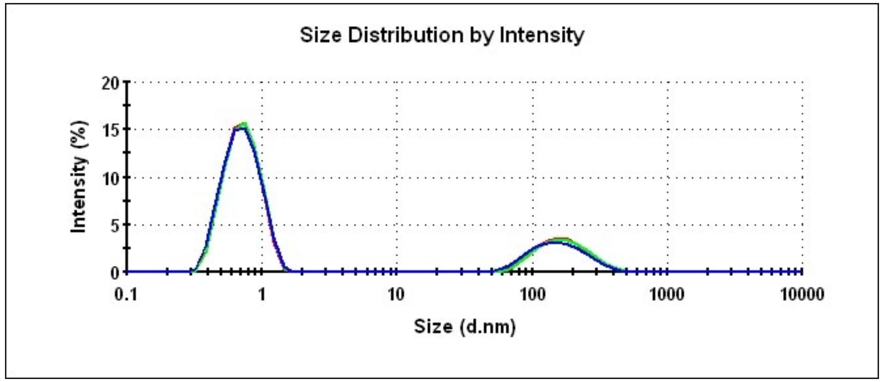
- Analysis dominated by ensemble scattering techniques;
  - Dynamic Light Scattering (DLS).
  - Small angle X-ray Scattering (SAXS).
  - Ensemble *averaging*.
  - Model based.



SAXS



DLS

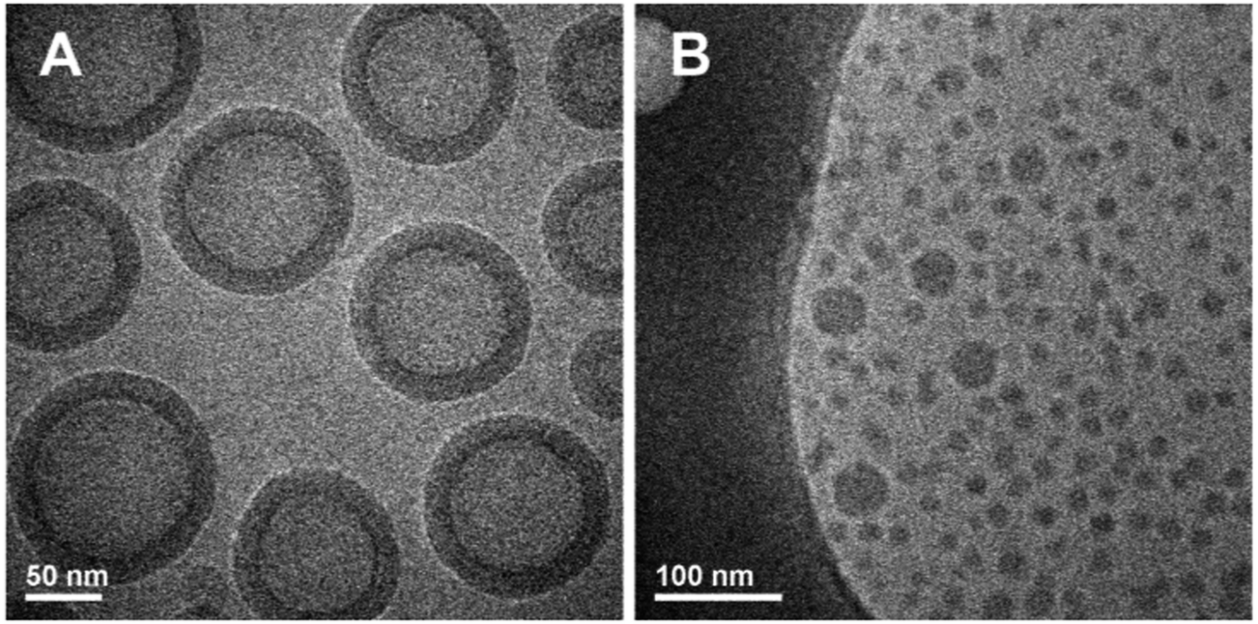


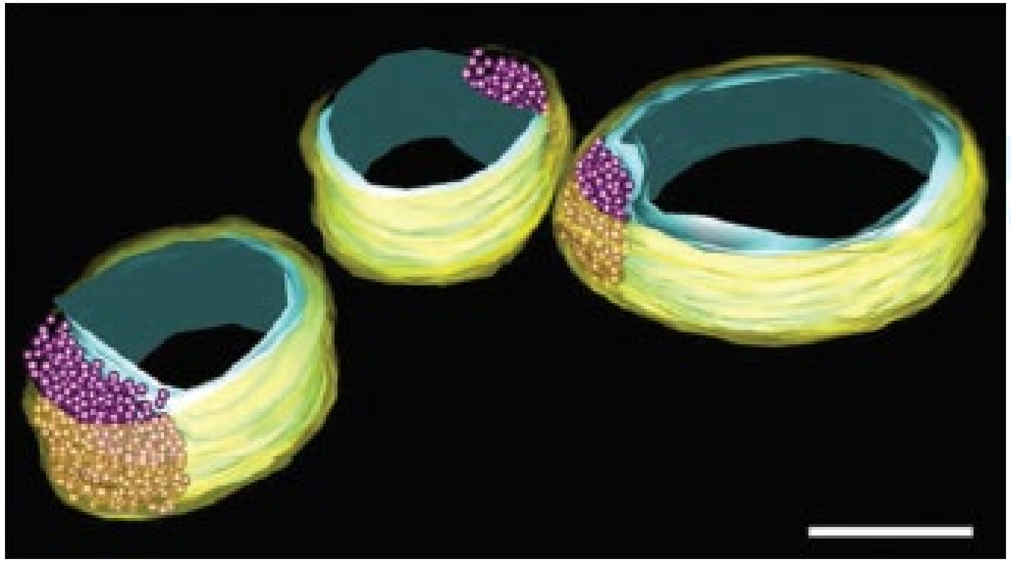
Cryo-TEM of Soft Matter

- Cryo-TEM reduces e$^-$ beam damage and allows for characterization of soft matter and nanomaterials in a native, frozen-hydrated (or solvated!) state.

- Provides a direct, *real-space*, visual representation of individual soft structures.

- 'Fixes' the sample in place, allowing for in-depth structural and <u>interfacial</u> investigation.

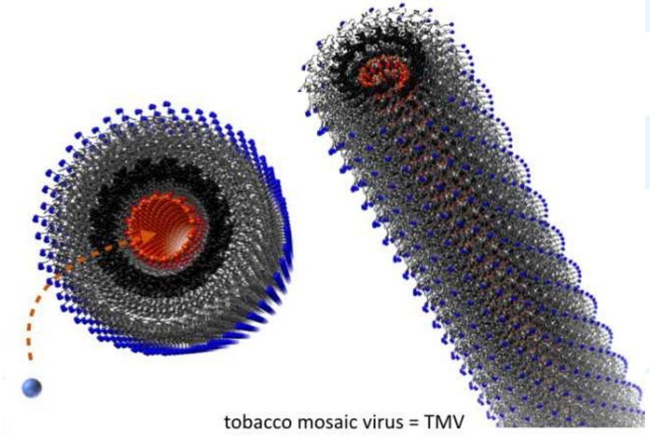




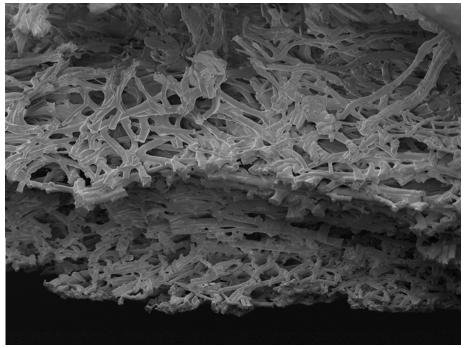
Bonnaud, C. *et. al.* ACS Nano 2014, 8, 3451-3460.
S. A. Meeuwissen, *et. al.*, Polym. Chem. 2014, 5, 489-501.

Soft Matter and Nanomaterials

- Biological based ‘soft’ nanoparticles e.g., viruses and polymer conjugates.



- Synthetic organic nanostructures e.g., polymers



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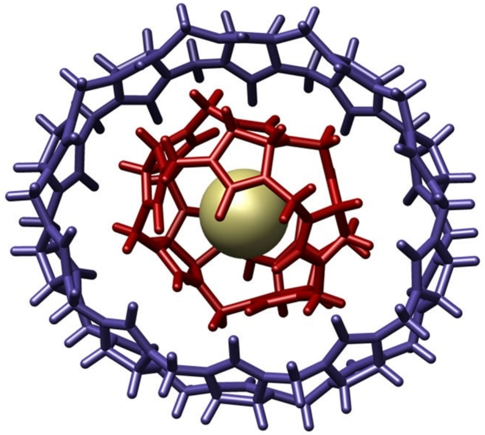

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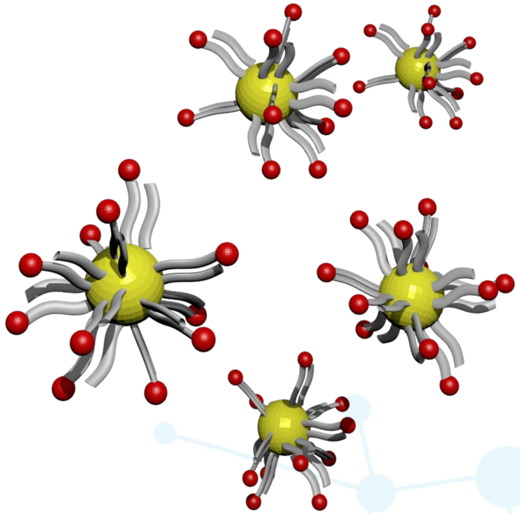
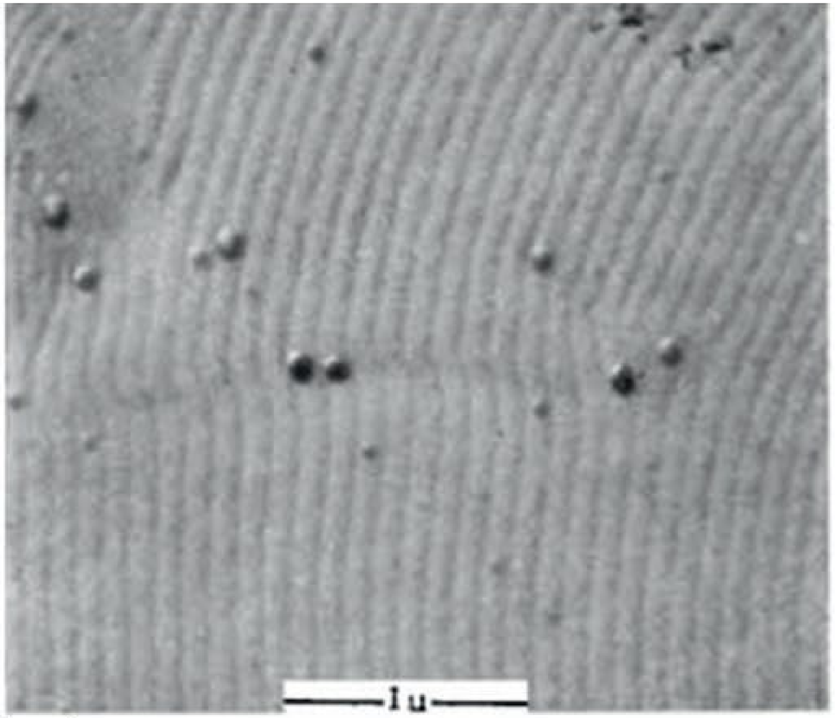


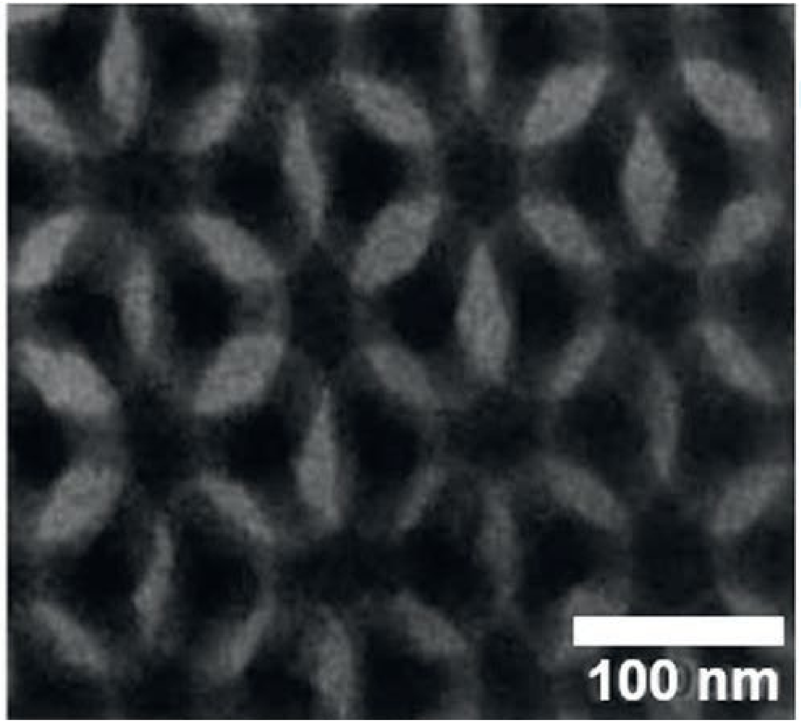
SYNTHETIC ORGANIC NANOSTRUCTURES

Synthetic Organic Nanostructures – The Early Years

- e^- beam damage in the TEM is still a definite factor.
- However, polymers can often survive a high vacuum environment.
- Room temperature scanning electron microscopy (SEM) and TEM were useful in the early understanding of block copolymers.



SEM micrograph of a phase separated diblock copolymer taken in 1966.[1]

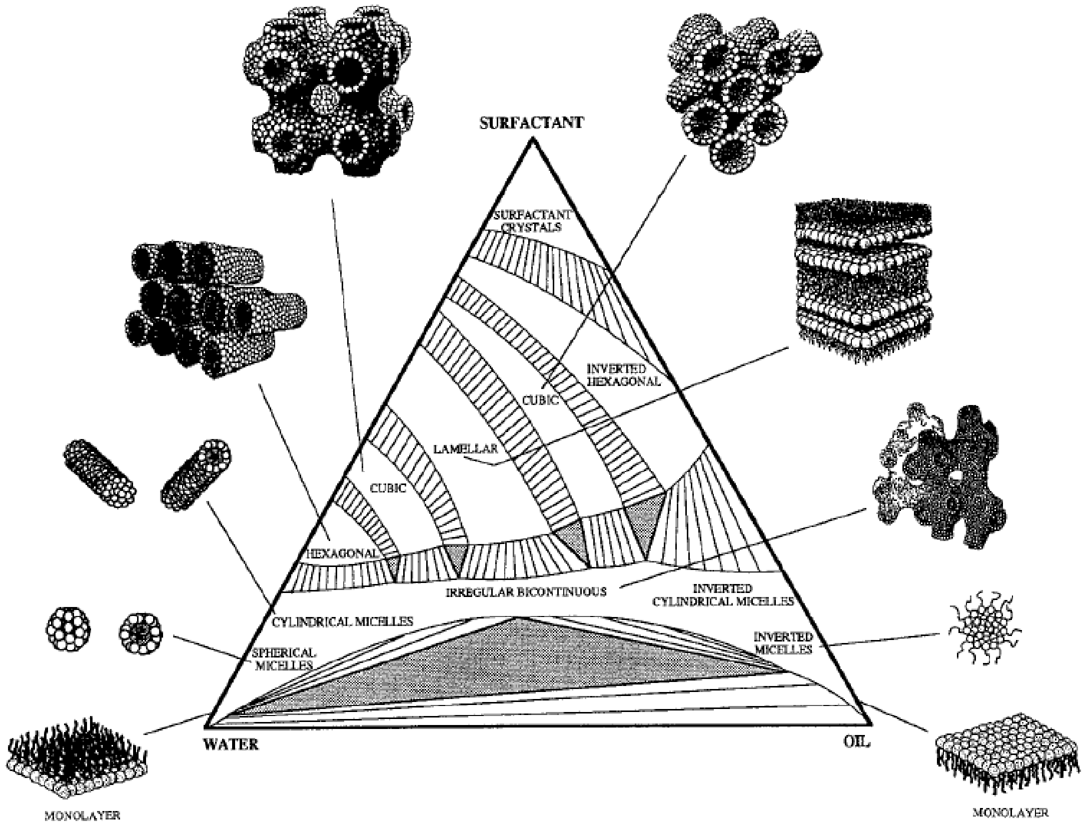


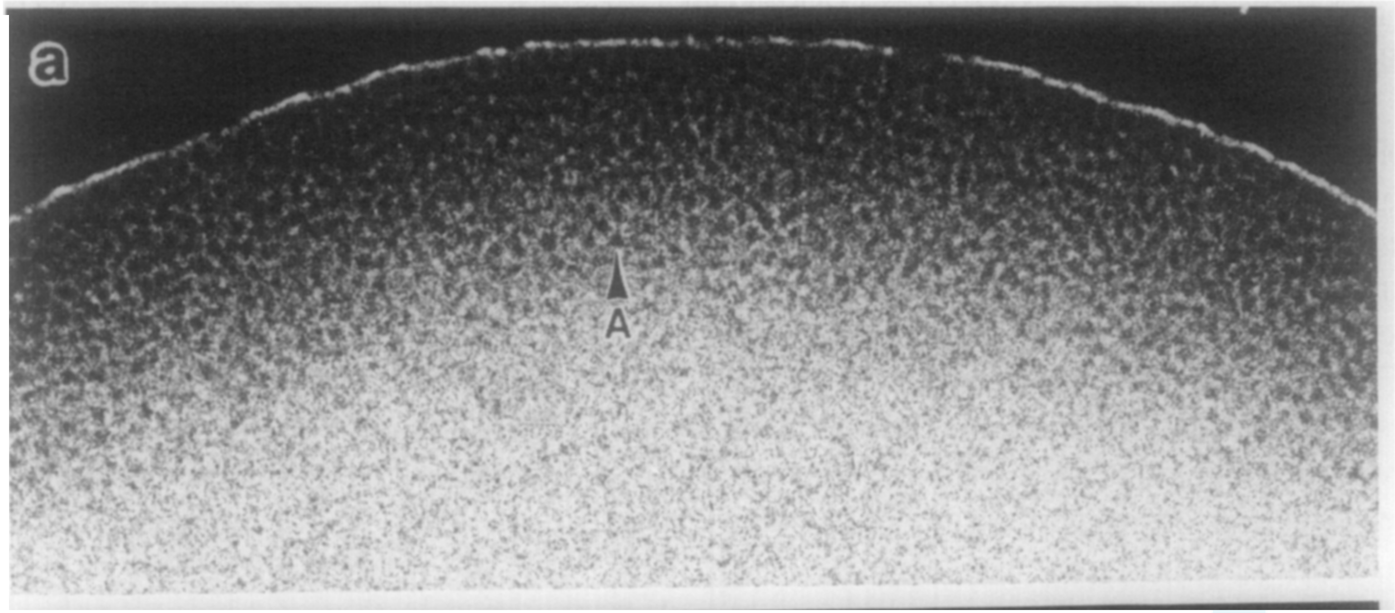
TEM micrograph of the 3D phase separation of a block copolymer taken in 1988.[2]

1. E. Vanzo, Journal of Polymer Science Part A-1: Polymer Chemistry 1966, 4, 1727-1730.
2. E. L. Thomas, *et. al* Nature 1988, 334, 598-601.

Synthetic Organic Nanostructures – The Early Years

- Micelles, Vesicles etc. from tri-phasic surfactant/oil/water mixtures were early candidates for cryo-TEM experiments.
  - Typically rely on scattering techniques (DLS, SAXS) due to artifacts from drying. .
  - Cryo-EM provided real space information to constrain scattering models.



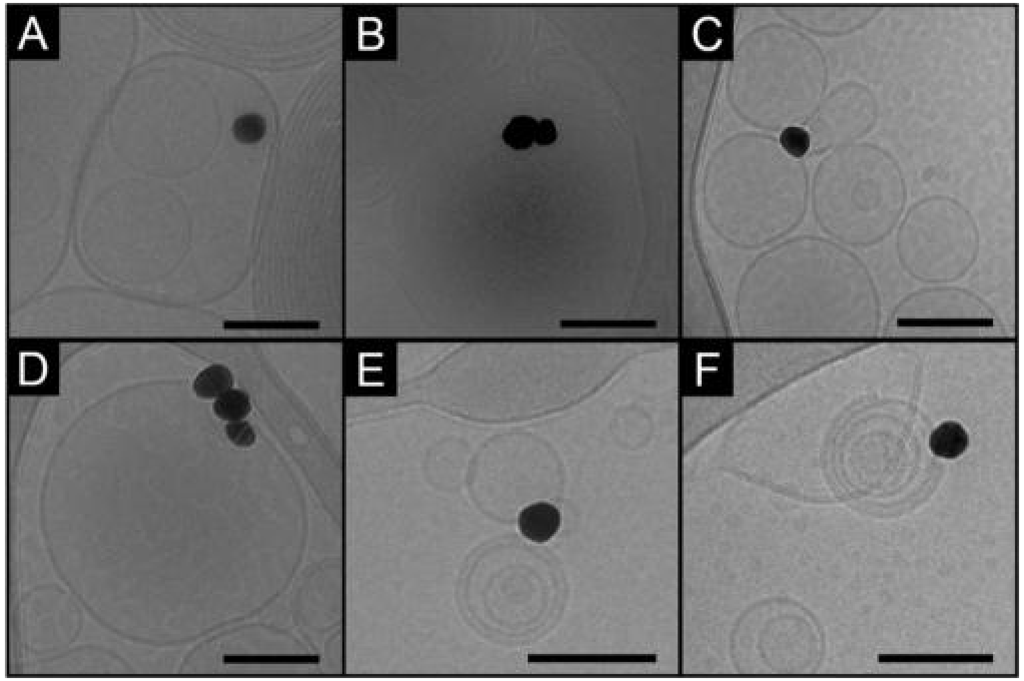


Early cryo-EM image of 1.0 wt% cetyltrimethylammonium bromide (CTAB) micelles swollen with toluene, imaged against a background of vitreous ice.

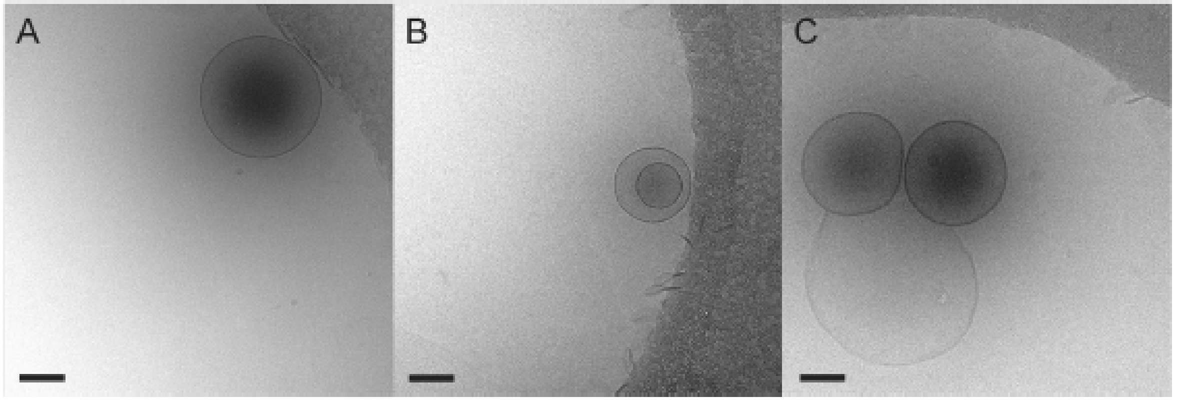
P. K. Vinson, *et.al* J. Colloid Interface Sci. 1991, 142, 74-91.

Synthetic Organic Nanostructures

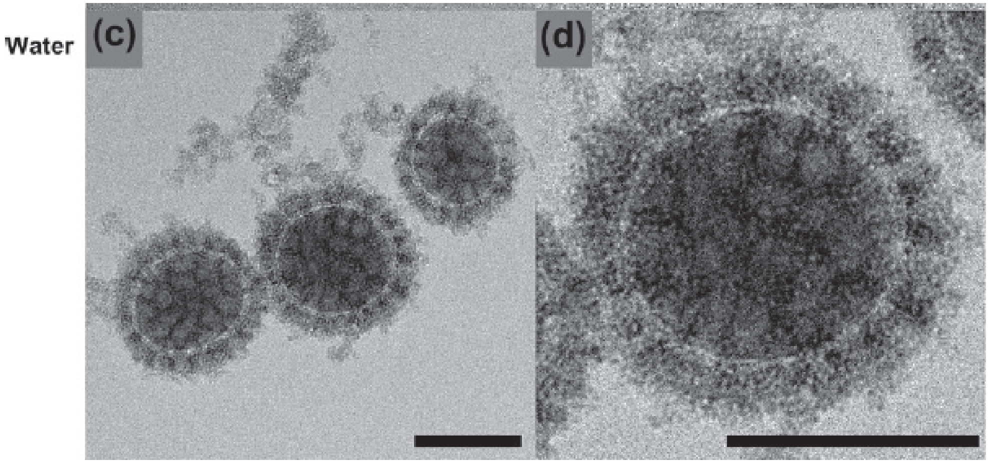
Liposomes and citrate-stabilized gold nanoparticles.



Cross-linked nanobubbles of perfluorocarbon.



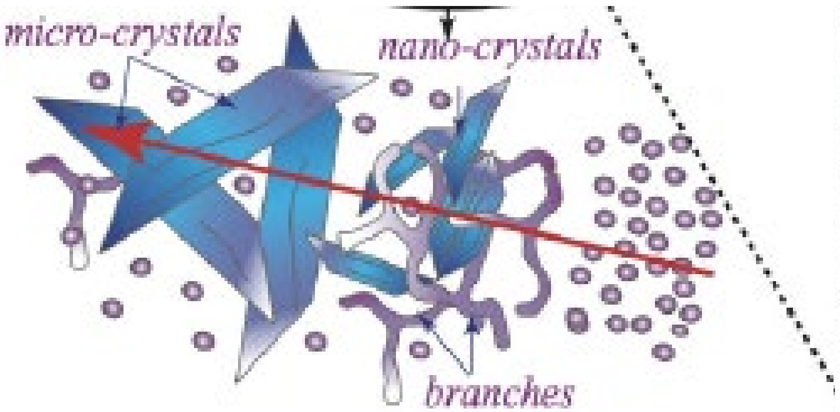
Mixed poly(acrylic acid) (PAA)/polystyrene (PS) brush-grafted silica nanoparticles

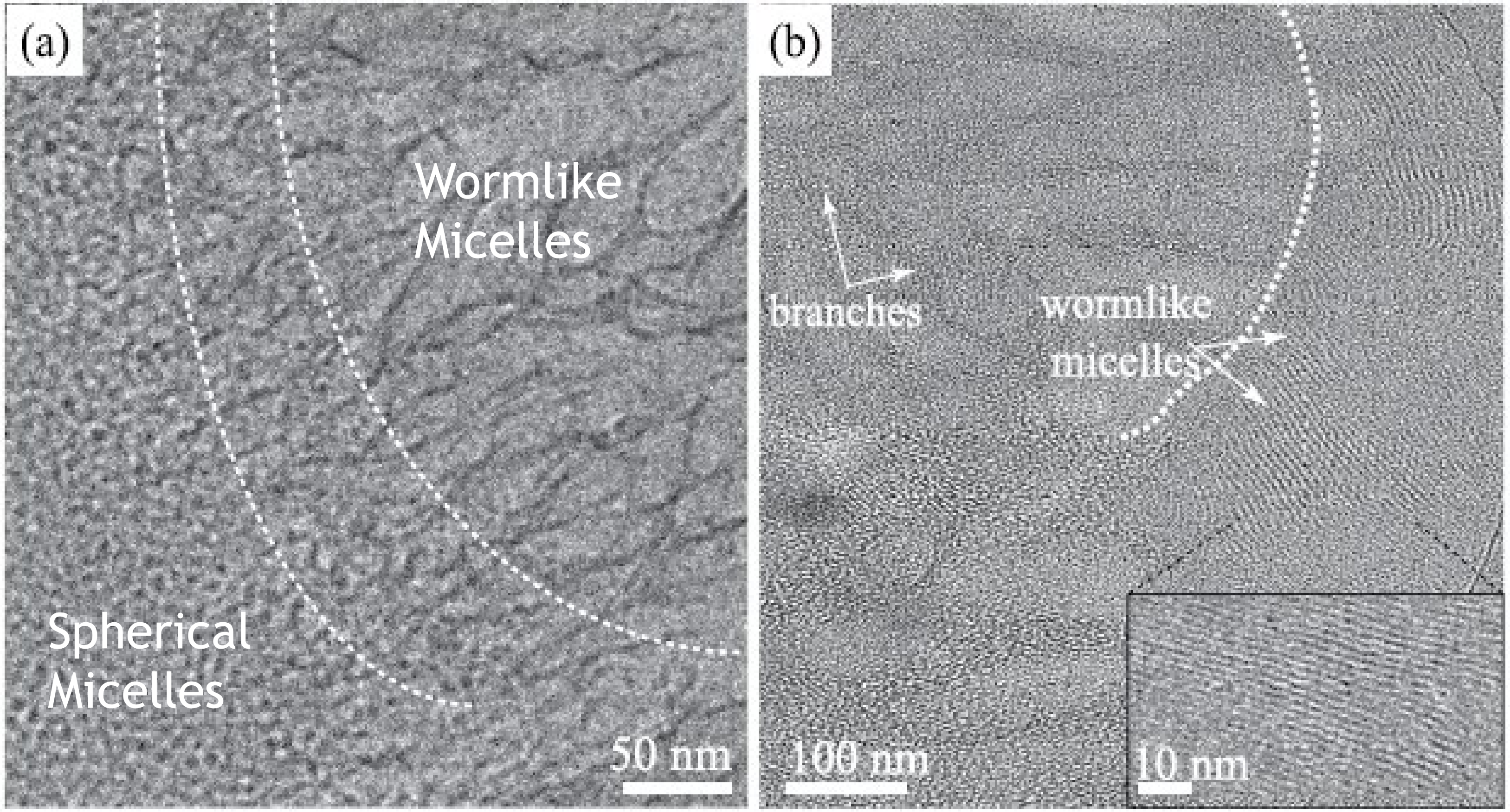


V. Zivanovic, *et. al.* J Phys Chem Lett 2018, 9, 6767-6772.
C. Hernandez, *et. al.* Scientific Reports 2017, 7, 8.
T. L. Fox *et al.* Langmuir 2015, 31, 8680-8688.

Synthetic Organic Nanostructures – Capturing Dynamics

- Now, cryo-EM can be used to observe a 'snapshot' of structural transitions in surfactant based systems.
    - Evolution of TWEEN-80 micelles.

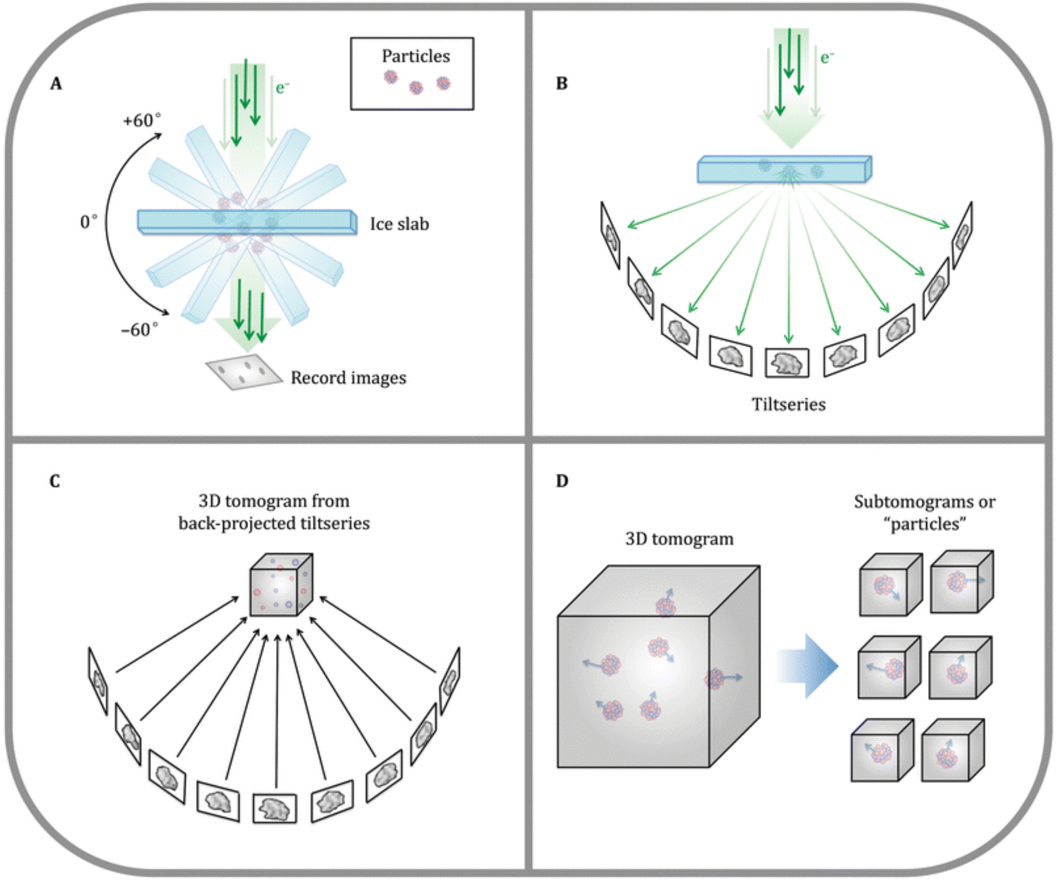


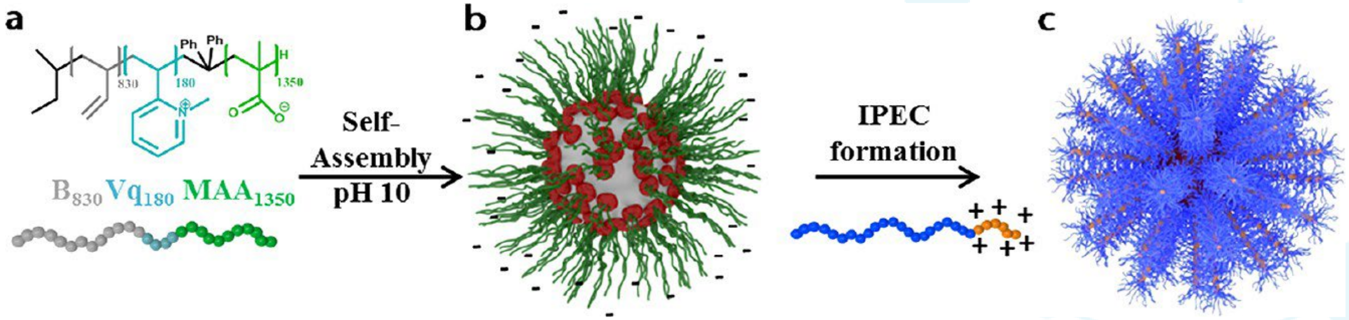


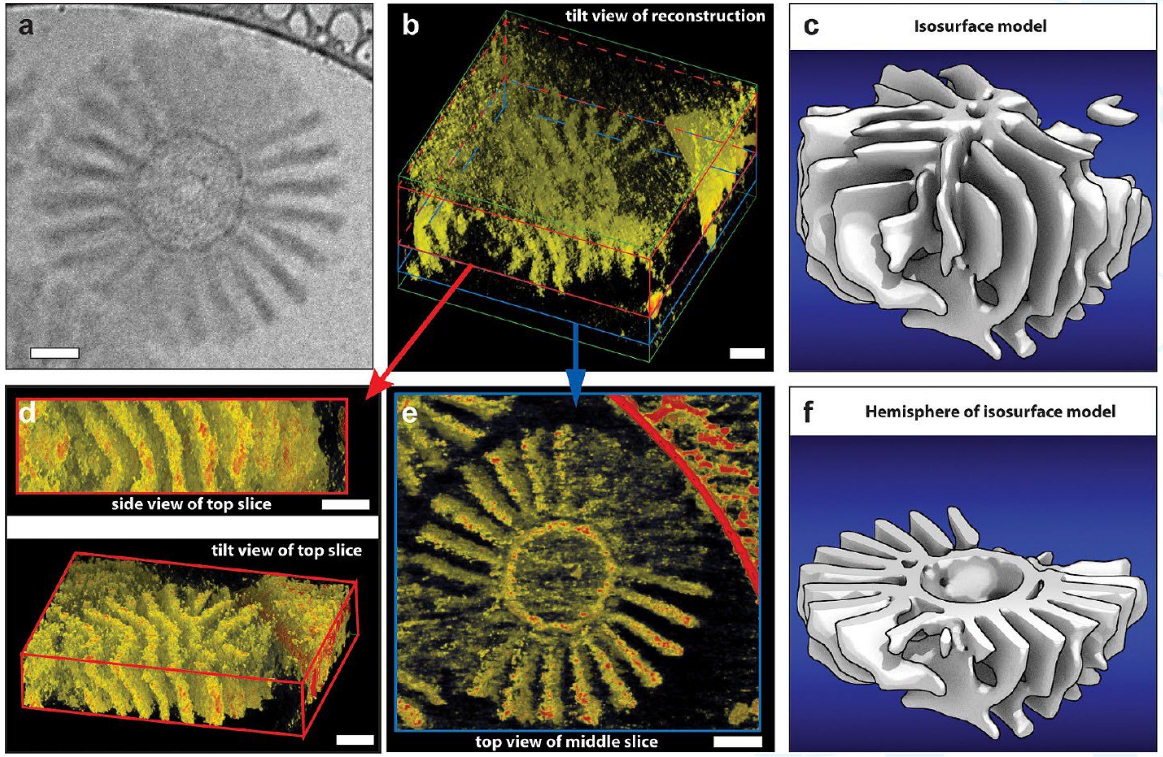
J. J. Cardiel, *et. al*. Scientific Reports 2015, 5, 17941.

Cryo-Electron Tomography (Cryo-ET)

- Allows visualization of the 3D structure of self-assembled systems.
- A series of images are taken at different tilt angles that lead to a 3D computed structure.



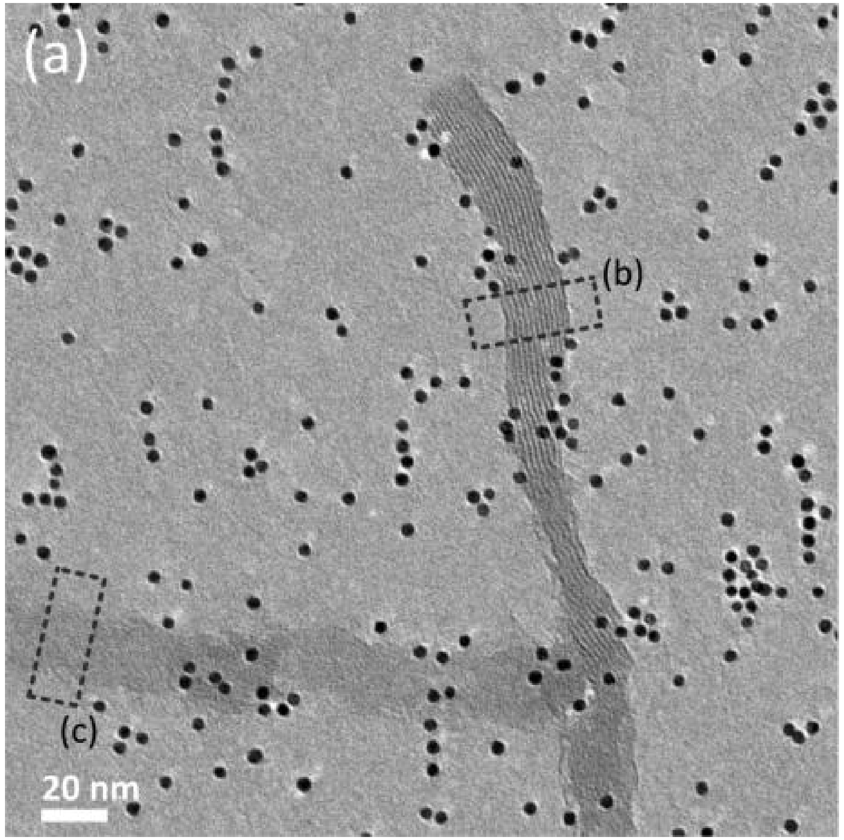




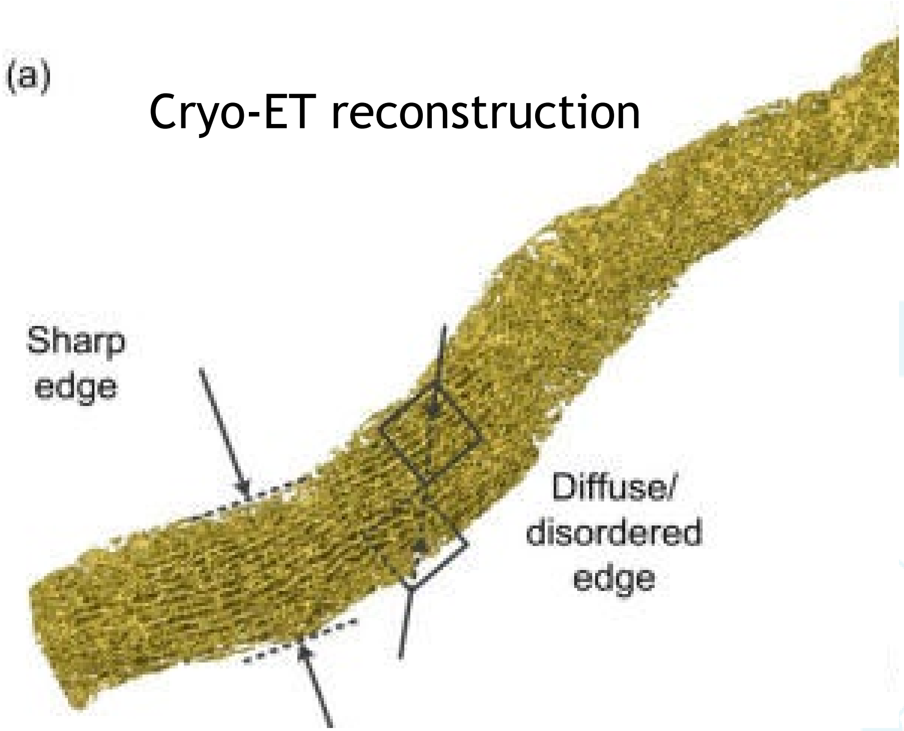
T. I. Lobling *et al.*, ACS Nano 2014, 8, 11330-11340.
J. G. Galaz-Montoya, S. J. Ludtke, Biophys Rep 2017, 3, 17-35.

Solvated Organic Nanostructures

- Poly(3-hexylthiophene) (P3HT) assemblies in vitrified organic solvents were visualized at nanometer scale



Cryo-TEM image of two P3HT wires vitrified in *ortho*-Dichlorobenzene.



Performed cryo-TEM in toluene and o-DCB.

M. J. M. Wirix, *et. al*. Nano Lett. 2014, 14, 2033-2038.

INORGANIC NANOMATERIALS

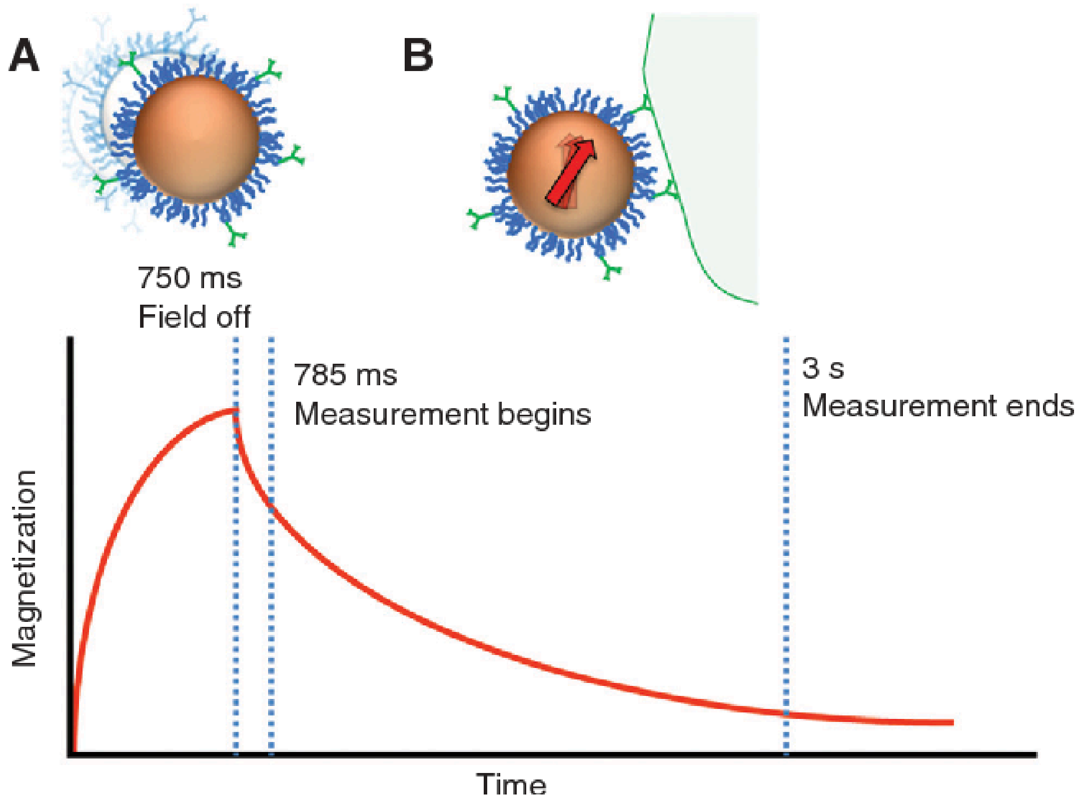
Cryo-TEM of Magnetic Nanoparticle Assemblies

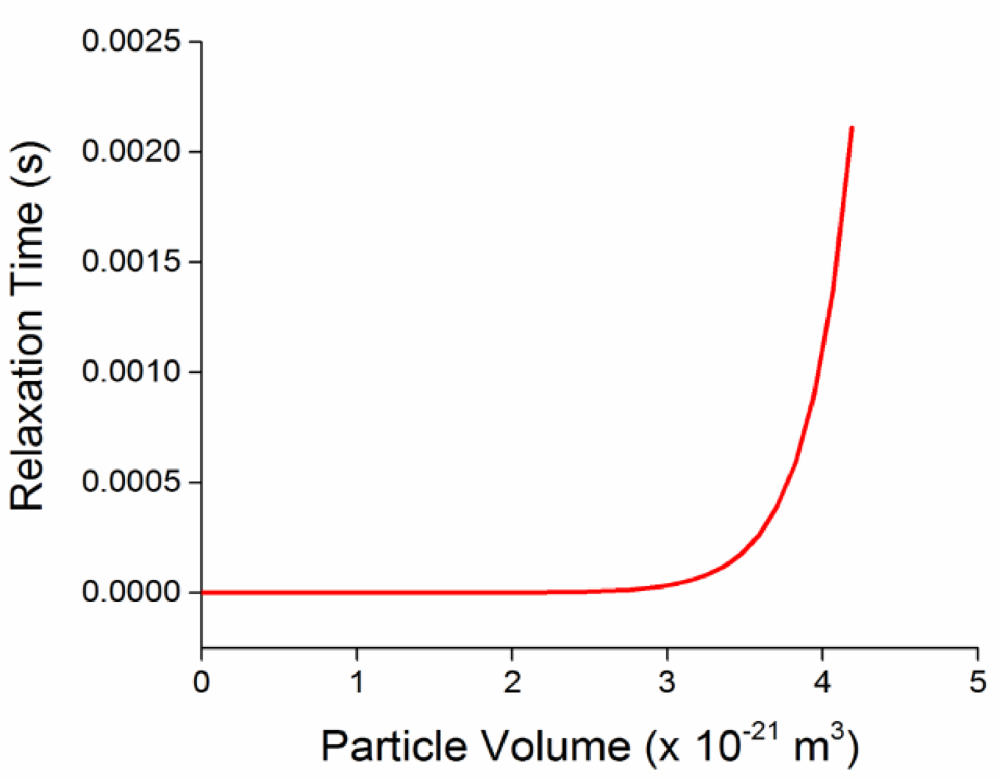
Magnetic Nanoparticle Relaxation

Magnetite (Fe_3O_4) NPs for Cancer Detection using Magnetic Relaxometry

$$\tau = \tau_0 e^{\left(\frac{KV}{k_B T}\right)}$$

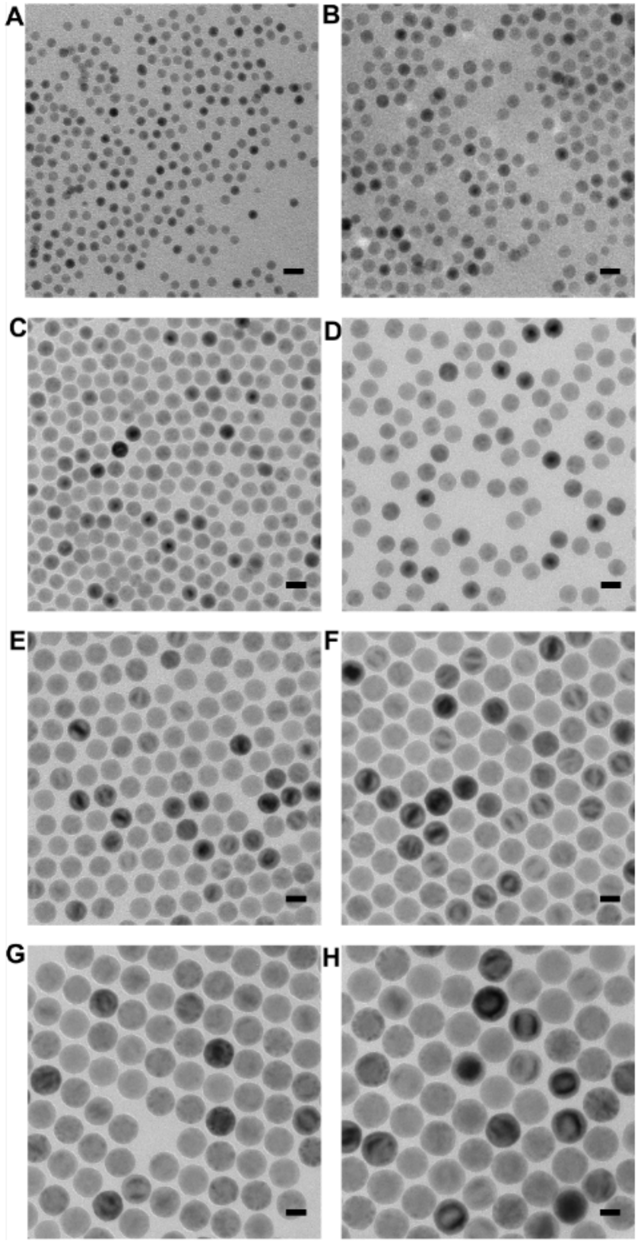
Neél Relaxation $\propto e^V$

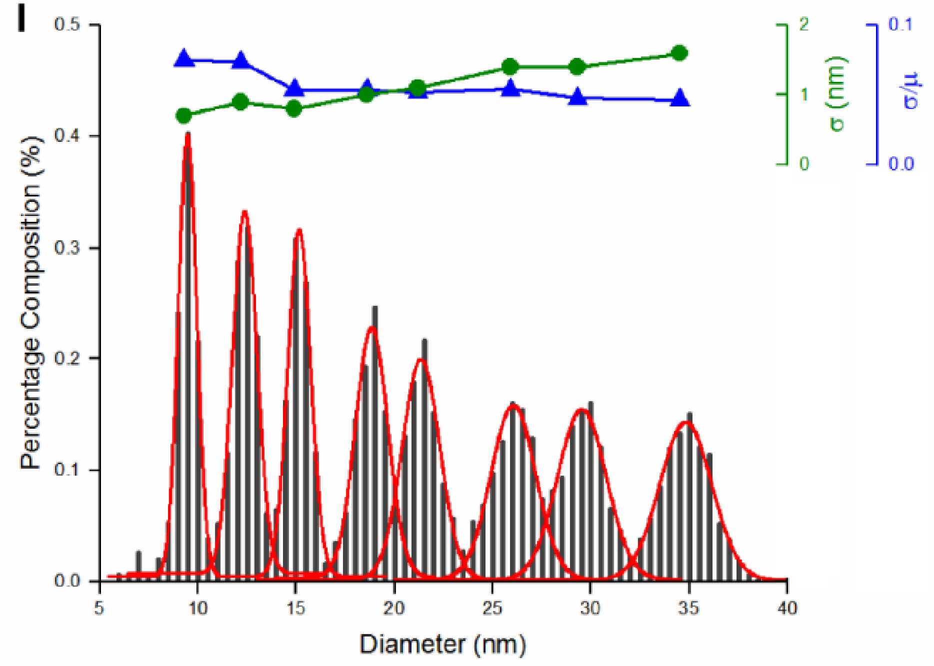




L. P. De Haro et. al. Biomedical Engineering / Biomedizinische Technik, 2015, 60, 445.

Magnetite (Fe_3O_4) NPs – Control of Size, Size Distribution





Nanoparticles sizes are 9.3 ± 0.7 nm to 34.5 ± 1.6 nm in size.

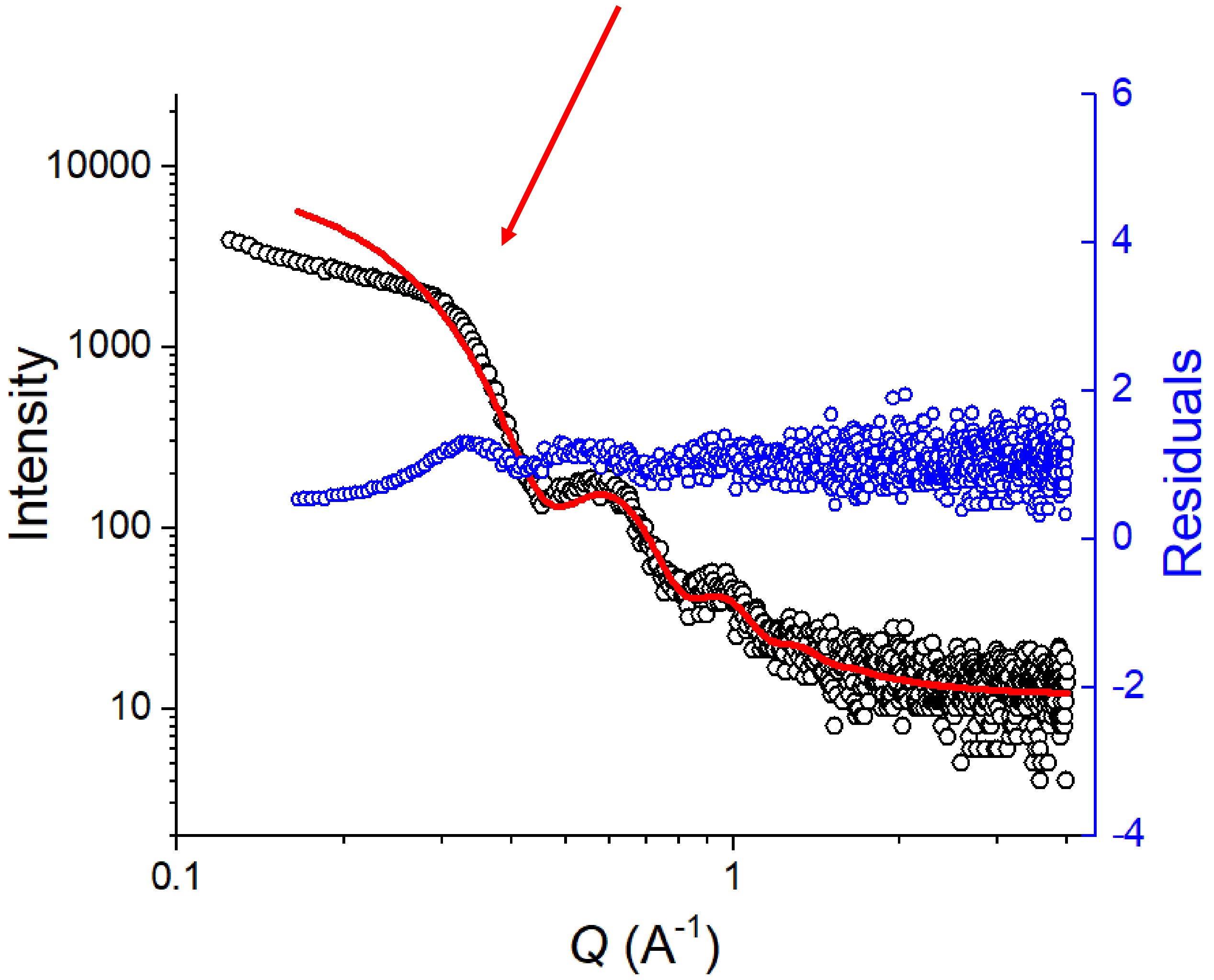
Coefficient of variation = 0.066.

M_{sat} ~ 70 Am^2/kg

Scale Bars = 20 nm

E. C. Vreeland et. al. Chem. Mater. 2015, 27, 6059-6066.

Small Angle X-Ray Scattering (SAXS)



Small Angle X-ray Scattering (SAXS)

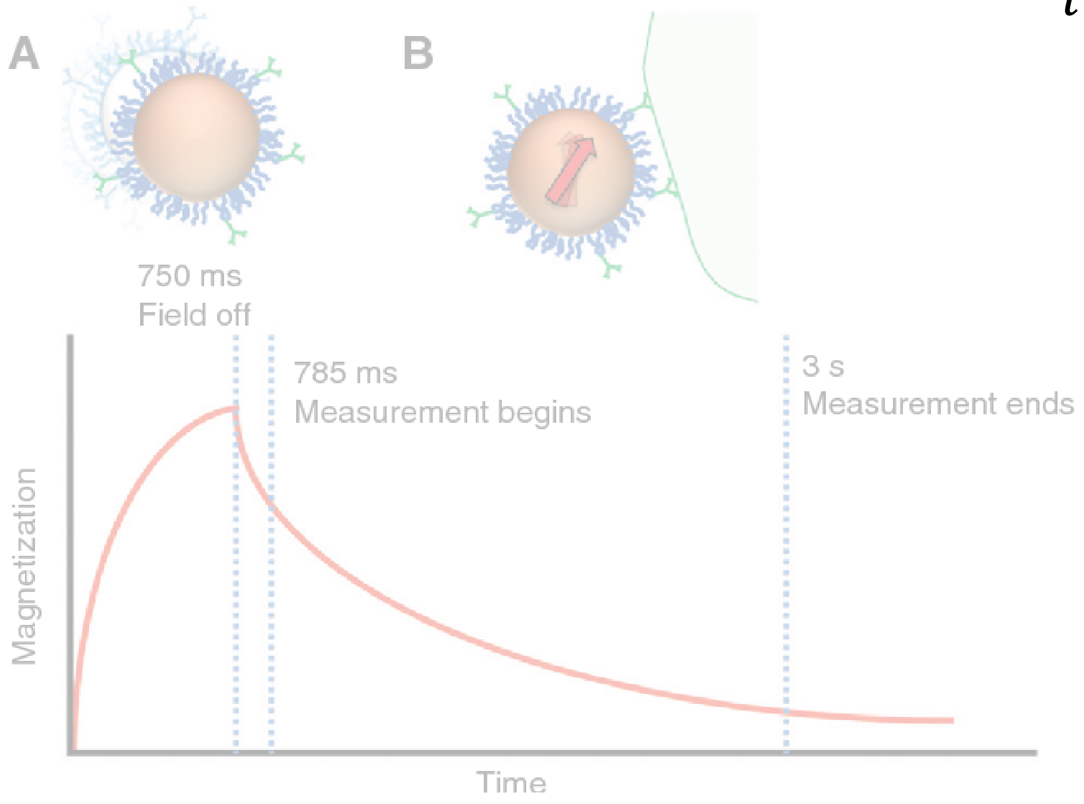
Deviation from model fit indicates particle interactions.

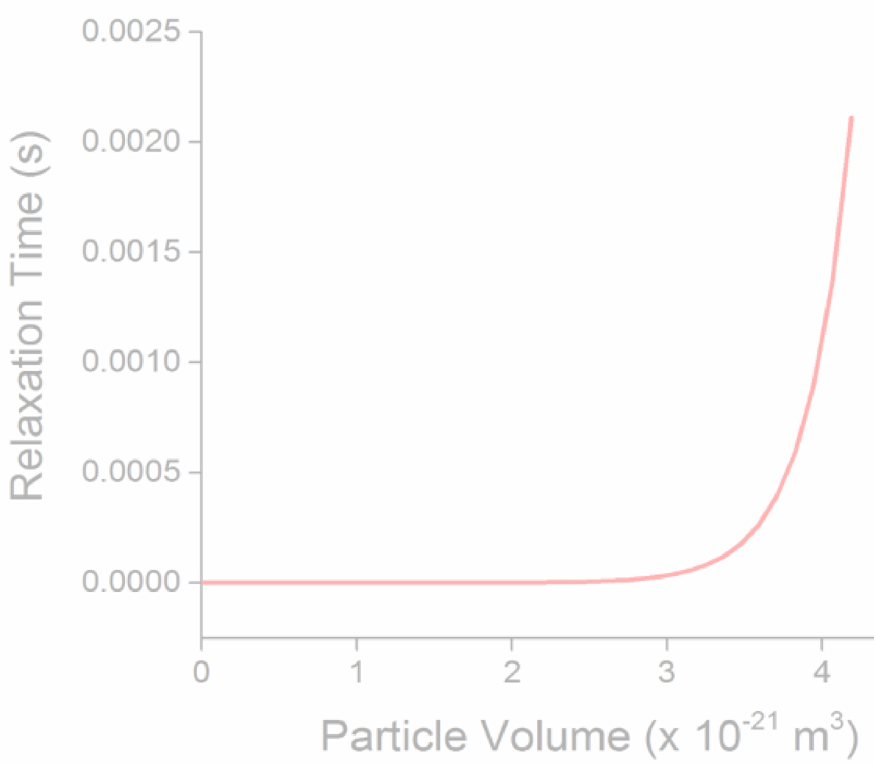
Magnetic Nanoparticle Relaxation

Magnetite (Fe_3O_4) NPs for Cancer Detection using Magnetic Relaxometry

$$\tau = \tau_0 e^{\left(\frac{KV}{k_B T - T_0}\right)}$$

Dipolar Interactions





L. P. De Haro et. al. Biomedical Engineering / Biomedizinische Technik, 60, 2015, 445.

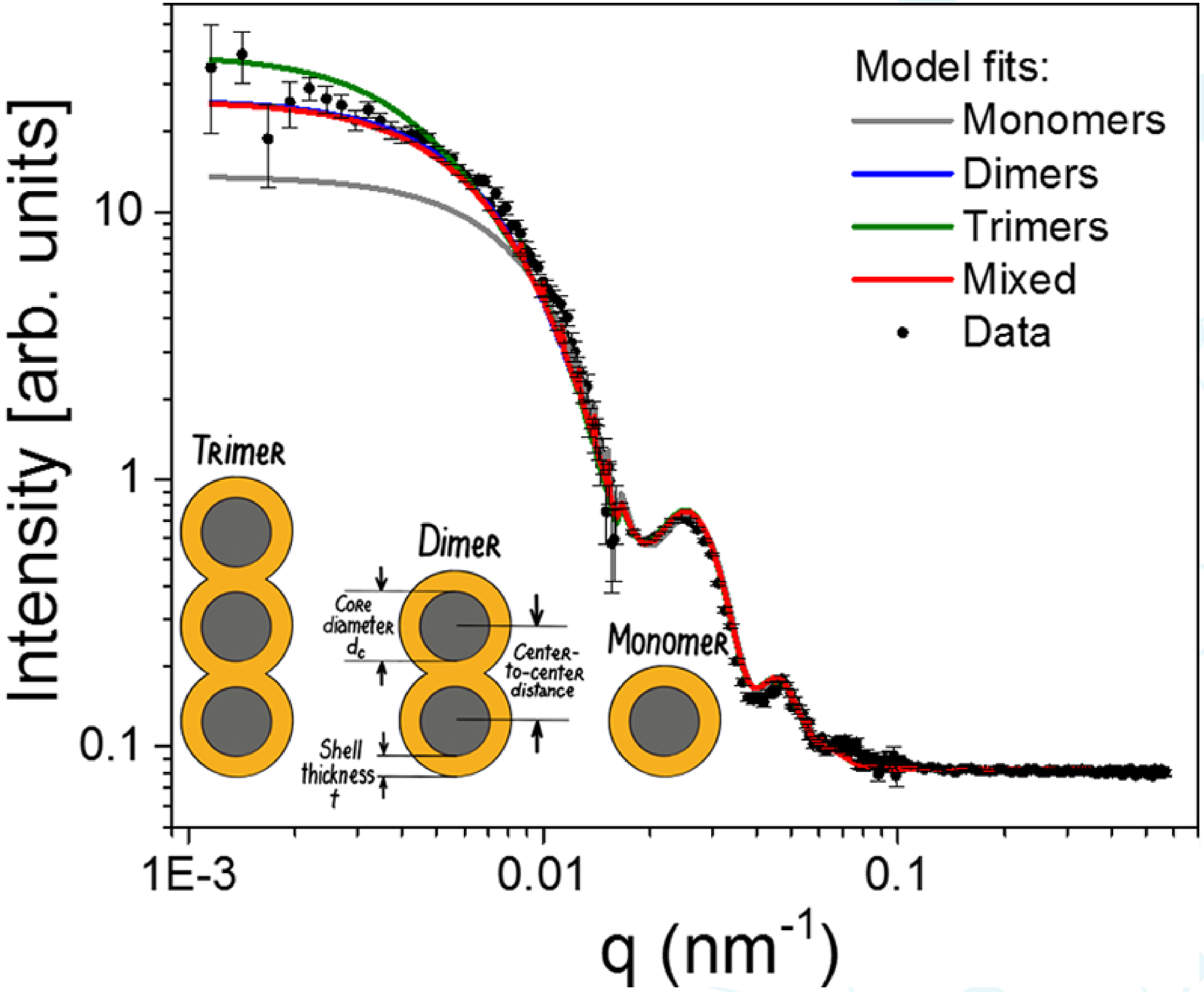
Small Angle Neutron Scattering (SANS)

Dispersed in water by surrounding in a hydrophobic polymer layer.

81 % vol fraction *dimers*.

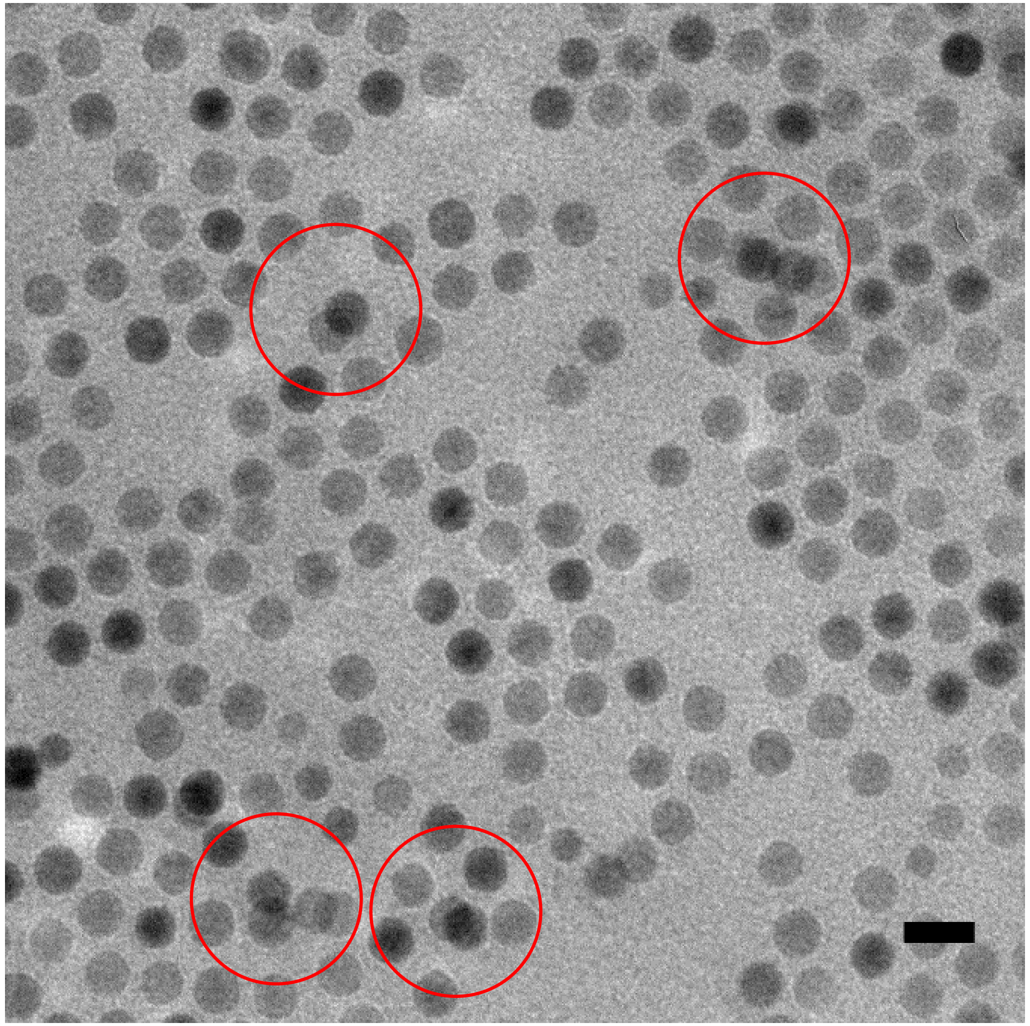
25.3 nm core diameter.
6.6 nm shell thickness.

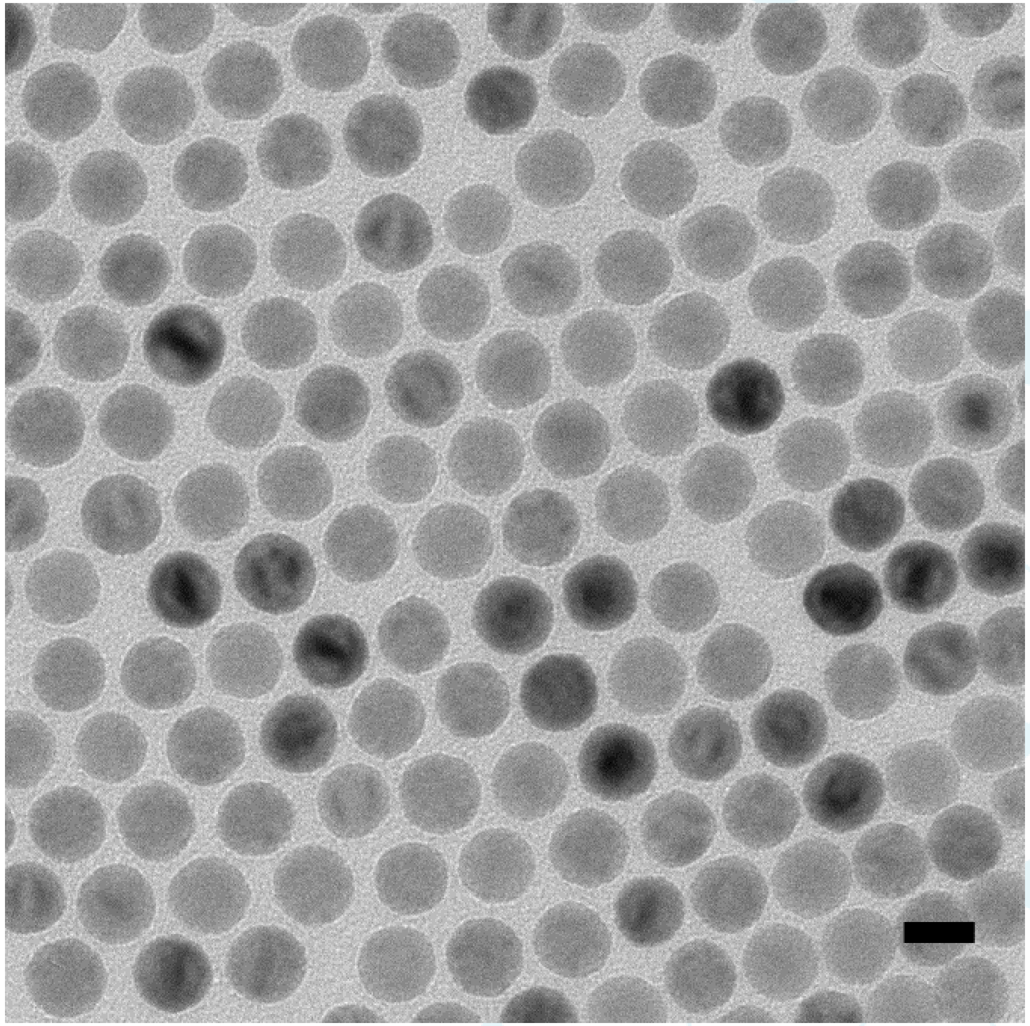
Interparticle spacing measured to be 8.8 nm.



K. Theis-Bröhl, *et al* ACS Applied Materials & Interfaces 2018, 10, 5050-5060.

TEM

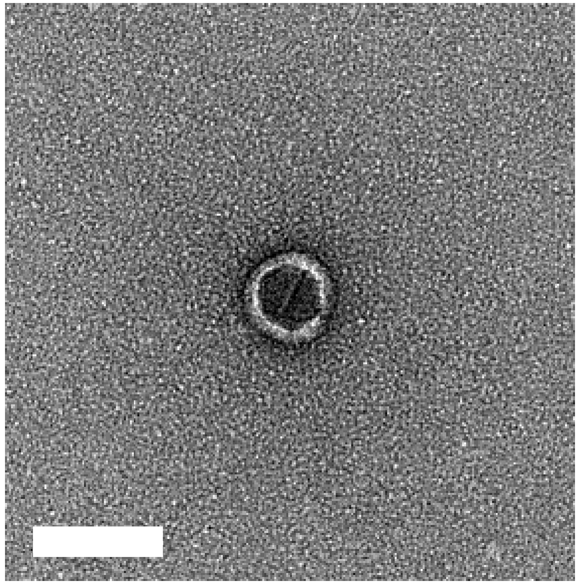


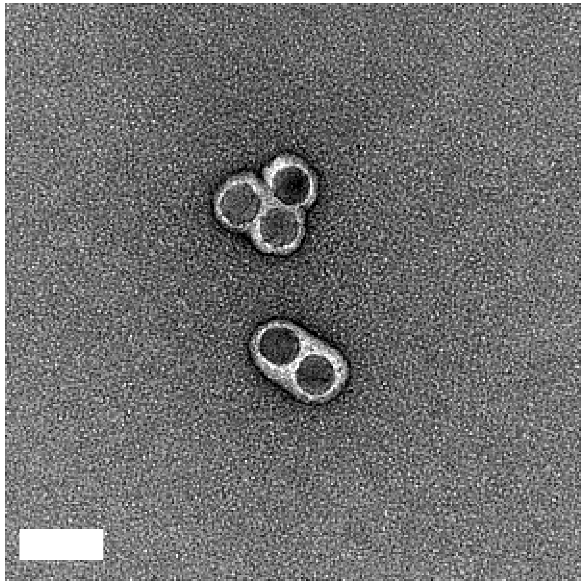


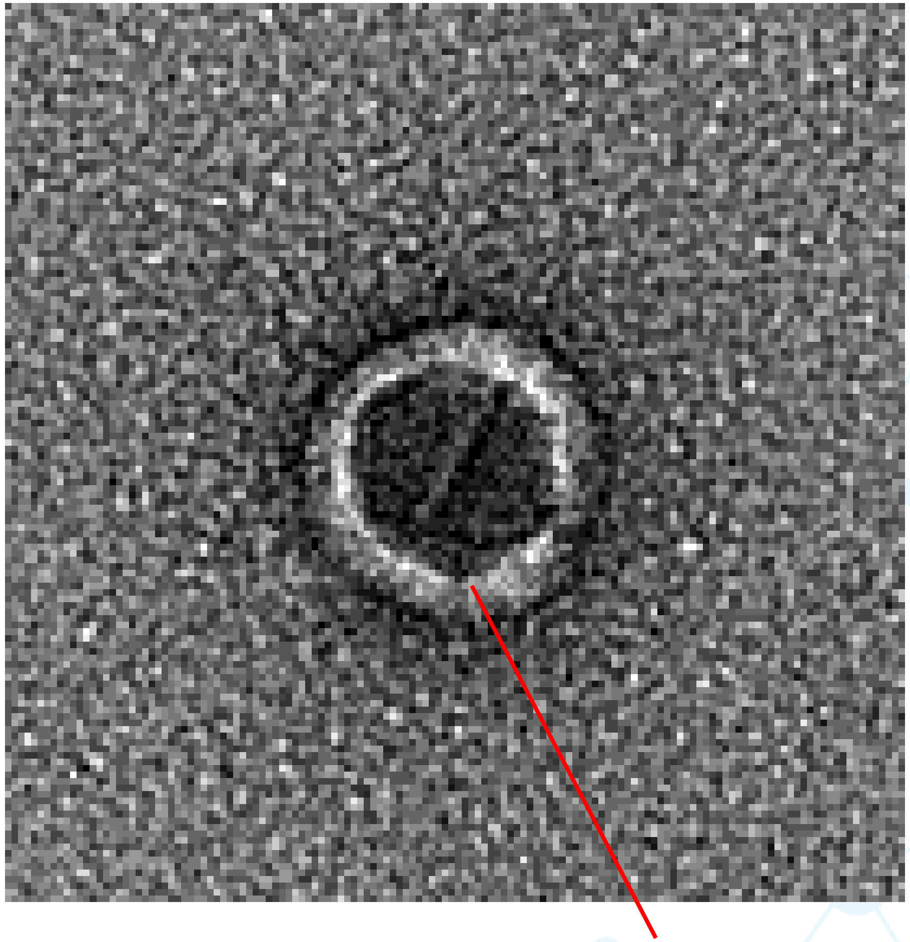
Drying effects can also change the strength of the magnetic interactions as the capping ligand de-solvates.

Negative Stain Experiments

- Staining using uranyl acetate to introduce contrast against the carbon background.
- Introduces artifacts to the system.
- Also does not eliminate drying effects.



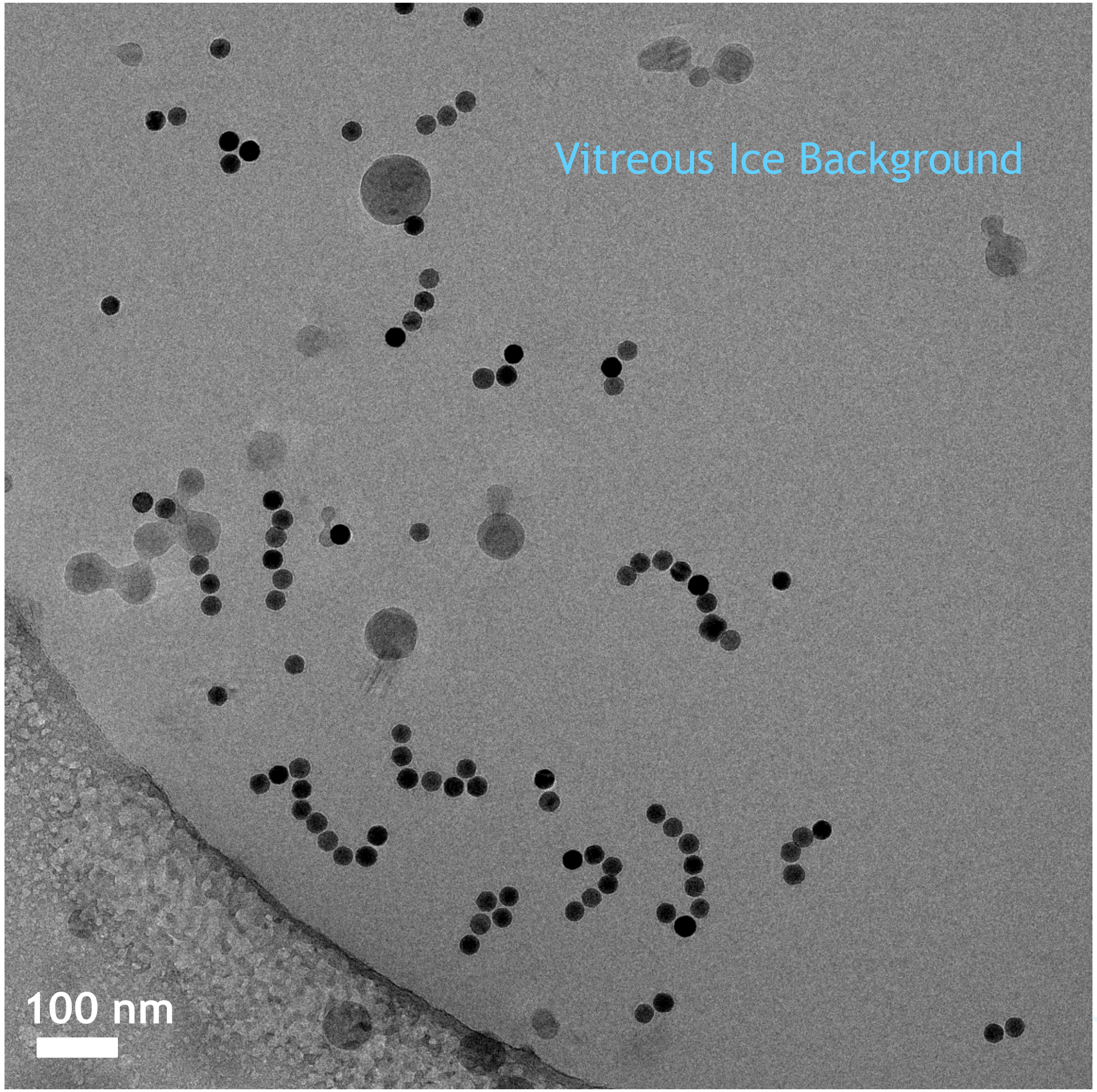




4.8 nm
cf. 6.6 nm from SANS

Scale Bars = 50 nm

Cryo-EM of Aqueous Suspension of Magnetite NPs



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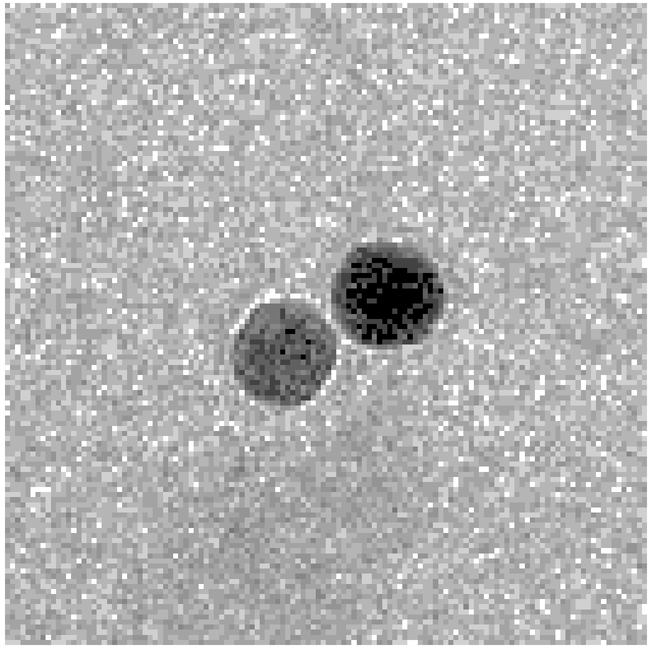
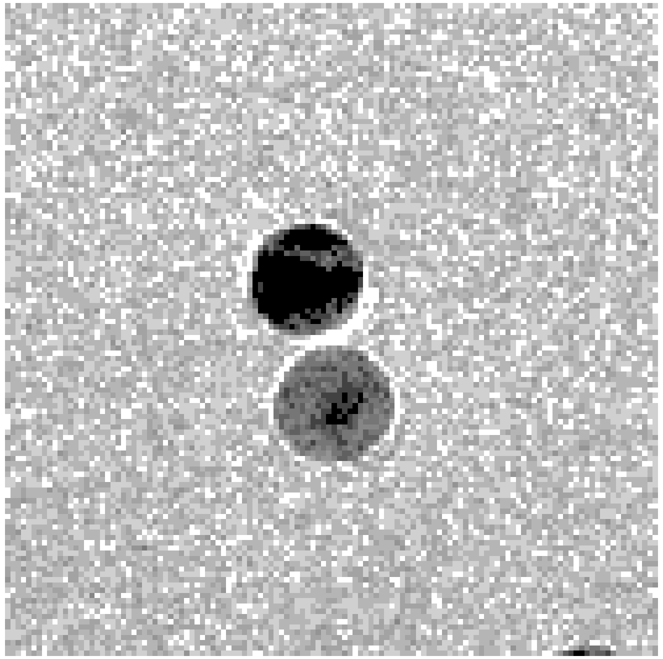
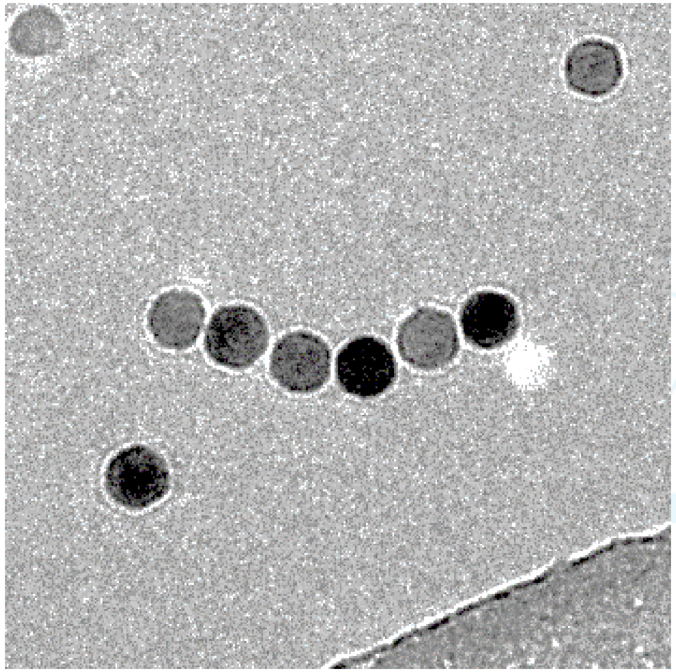




Magnetic Dimers



Chain Formation

- Cryo-TEM confirms the observations from SANS.
  - *Would not have been possible with conventional TEM!*

Thank you for your attention.

This work was performed, in part, at the Center for Integrated Nanotechnologies, an Office of Science User Facility operated for the U.S. Department of Energy (DOE) Office of Science. Sandia National Laboratories is a multimission laboratory managed and operated by National Technology & Engineering Solutions of Sandia, LLC, a wholly owned subsidiary of Honeywell International, Inc., for the U.S. DOE's National Nuclear Security Administration under contract DE-NA-0003525. The views expressed in the article do not necessarily represent the views of the U.S. DOE or the United States Government. Los Alamos National Laboratory, an affirmative action equal opportunity employer, is managed by Triad National Security, LLC for the U.S. Department of Energy's NNSA, under contract 89233218CNA000001.